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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,309	06/23/2003	John R. Carlson	YALE-039/01US	7963

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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 10/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/601,309	CARLSON ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-55* is/are pending in the application.

4a) Of the above claim(s) *38-50,54 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-37 and 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1) Claims 27 to 55 are pending in the instant application.

Election/Restrictions

2) Claims 38 to 50, 54 and 55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 05 April of 2006. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement with respect to these claims, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3) Claims 27 to 37 and 51 to 53, in so far as they relate to an amino acid sequence other than SEQ ID NO:24, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in correspondence filed 05 April of 2006. The traversal is on the ground(s) that, in accordance with M.P.E.P. 803.04 up to ten nucleotide sequences can be examined in a single application. Applicant is advised that this policy was discontinued several years ago because the nucleotide sequence databases have grown exponentially since the articulation of that policy. Further, Applicant's claims are not limited to nucleotide sequences. The claims recite amino acid sequences and because of codon degeneracy, they encompass potentially tens of thousands of different polynucleotides having different sequences.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

4) The information disclosure statement (IDS) submitted on 23 June of 2003 is in compliance with the provisions of 37 CFR 1.97 and has been considered by the examiner.

Drawings

5) The drawings in the instant application do not comply with 37 C.F.R. § 1.821(d), which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. Figures 3A to 3E, for example, describe a plurality of amino acid sequences without employting the required sequence identifiers. M.P.E.P. 2422.02 expressly states that "when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings".

Specification

6) The disclosure is objected to because it contains one or more embedded hyperlinks and/or other form of browser-executable code, for example, in line 20 on page 53 and in lines 16 and 22 on page 54. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01(p), which states that:

> "When a patent application with embedded hyperlinks and/or other forms of browser-executable code issues as a patent (or is published as a patent

application publication) and the patent document is placed on the USPTO web page, when the patent document is retrieved and viewed via a web browser, the URL is interpreted as a valid HTML code and it becomes a live web link. When a user clicks on the link with a mouse, the user will be transferred to another web page identified by the URL, if it exists, which could be a commercial web site. USPTO policy does not permit the USPTO to link to any commercial sites since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. If hyperlinks and/or other forms of browser-executable code are embedded in the text of the patent application, examiners should object to the specification and indicate to applicants that the embedded hyperlinks and/or other forms of browser-executable code are impermissible and require deletion."

Correction is required.

Claim Objections

7) Claims 51 to 53 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. A properly dependent claim can not conceivably be infringed without infringing any of the claims from which it depends. Claim 53, for example, is improper because it can be infringed by "an isolated nucleic acid molecule" that does not infringe the "isolated protein or polypeptide" of claim 40. See M.P.E.P. 608.01(n)III.

8) Each of claims 33 and 36 are objected to under 37 CFR 1.75 as being a substantial duplicate of each of claims 32 and 35, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same

thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9) Claims 27 to 37 and 51 to 53 are rejected under 35 U.S.C. § 101 because they are drawn to an isolated nucleic acid molecule with no apparent or disclosed specific and substantial credible utility in currently available form. The instant application has provided a description of a plurality of amino acid sequences belonging to a group of proteins each of which is identified therein as a Drosophila odorant receptor (DOR), a putative odorant receptor of insect origin, and isolated nucleic acid encoding each of those proteins. The instant application does not identify a particular compound or class of compounds that activate the elected species of DOR (SEQ ID NO:24) nor does it disclose with specificity the consequence of that activation.

The text on page 15 of the instant specification states that "members of the [DOR] family of proteins can be used: 1) to identify agents which modulate at least one activity of the protein; 2) to identify binding partners for the protein, 3) as an antigen to raise polyclonal or monoclonal antibodies, and 4) in methods to modify insect behavior". These activities essentially serve to further characterize the claimed invention and do not constitute specific and substantial utilities because no specific utility has been disclosed for "binding partners", agents which modulate" and "antibodies" that bind to

the DOR protein encoded by the claimed nucleic acid. The assertion that one can employ a DOR protein "in methods to modify insect behavior" would not be accepted as credible by one of ordinary skill in the art of receptor biology because a DOR protein of the instant invention is a member of the G protein-coupled receptor family, each of which has a complex serpentine structure comprising four extracellular and intracellular domains divided by seven transmembrane domains. There is no evidence of record that any member of this structurally complex membrane-associated protein family has ever successfully been exogenously administered to an organism to achieve a desired behavioral effect.

A process of identifying an agent that modulates the activity of the DOR protein encoded by the elected invention lacks specific and substantial utility in currently available form, because the instant specification fails to disclose the nature of the physiological response elected in an insect by the activation of the elected DOR. One of ordinary skill in the art readily appreciates the fact that certain compounds are going to attract insects by activating one or more specific odorant receptors while other compounds will repel them by activating one or more different receptors. This position is supported by the text on page 49 of the instant application and the statement in the third paragraph on page 376 of the Karg et al. publication (Karg & Suckling, 1999, INSECT OLFACTION (1999), Hansson (editor), Springer-Verlag, cited by Applicant) that "[v]arious fragrances are attractant or repellant to insects". Therefore, before a protein comprising the amino acid sequence presented in SEQ ID NO:24 of the instant application can be used to identify a compound that attracts or repels an insect, one

must first engage in the experimentation needed to determine precisely what effect the agonist activation of that protein has on insect behavior. It is a matter of law that an invention must have a specific and substantial utility "in currently available form", which precludes the need for further research, if that research is needed to establish a utility for the claimed invention (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)), In the instant case, one can not employ a DOR protein of the instant invention in the specific, substantial and practical application of identifying compounds that attract or repel insects until one has first determined what effect the activation of DOR has on the behavior of an insect. Until one knows if an agonist of DOR is an attractant or a repellant, the putative receptor protein can not be employed in the specific application of identifying an attractant or a repellant. Because this additional experimentation is required before the claimed nucleic acid can be employed in a specific manner, the claimed invention lacks a specific and substantial practical utility in currently available form.

It is clear from the instant specification that the elected species of receptor protein described therein is what is termed an "orphan receptor" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility in the identification of compounds that have a specific influence of insect behavior. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. Whereas one could readily employ a putative receptor protein

of the instant invention in an assay to identify ligands thereto the information obtained thereby would be of little use until one discovers what effect that activation or inhibition of that protein is going to have on an insect. Because the instant specification has failed to credibly identify a specific physiological response which has been shown to be influenced by the activation or inhibition of a putative receptor protein of the instant invention an artisan would have no way of predicting what effects the administration of that ligand to an organism would have. If one can not predict the effects that the administration of a ligand of the putative receptor of the instant invention is going to have on an organism then it is unclear as to what practical benefit is derived by the public from the identification of that ligand.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and until a process is refined and developed to this point-where specific benefit

exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to an isolated nucleic acid encoding a DOR protein of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the elected species of DOR protein, or the gene encoding it, the instant invention is incomplete. To employ the DOR protein encoded by the claimed nucleic acid "to identify agents which modulate at least one activity of the protein", "identify binding partners for the protein" or "as an antigen to raise polyclonal or monoclonal antibodies", as suggested by the text on page 15 of the instant specification, is to employ that nucleic acid and the protein encoded thereby as the object of further research. In the absence of a knowledge of the natural ligands or biological significance of the DOR protein encoded by the claimed nucleic acid, there is no immediately obvious patentable use for that nucleic acid or the protein encoded thereby. To employ a DOR protein of the instant invention in the identification of substances which inhibit or induce its activity is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a specific and substantial practical use for the elected DOR then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10) Claims 27 to 37 and 51 to 53 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

11) Claims 27, 28, 31 to 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. These claims are single means claims because they encompass any isolated nucleic acid molecule encoding any protein having the activities recited therein, in the complete absence of any recited structural elements that provide the recited activities..

A single means claim, i.e., where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. In re Hyatt , 708 F.2d 712,>714 - 715,< 218 USPQ 195>, 197< (Fed. Cir. 1983) (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor.). When claims depend on a recited property, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See M.P.E.P. 2164.08(a)

12) Claims 27, 28, 31 to 37 and 51 to 53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. These claims encompass subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims encompass a nucleic acid encoding a protein or fragment thereof having other than the entire native amino acid sequence recited in claim 30 of the instant application wherein that protein or fragment thereof "causes the firing of an olfactory neuron when stimulated". *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Because the instant specification does not identify those amino acid residues in the amino acid sequence of a native DOR protein which are critical to the structural and functional integrity of that receptor protein, identify a structurally analogous protein for which this information is known and could be applied to the instant protein by

extrapolation, or even provide a single working example of an intentionally modified DOR protein of the instant invention, an artisan can not change even a single residue within the amino acid sequence of a native DOR protein and predict the effects of that change on the performance of that protein "by resort to known scientific law".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13) Claims 27 to 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13.1) Claim 27 is confusing because it is unclear if the first occurrence of the term "fragment thereof" is referring to the nucleic acid or the protein. The recitation of the term "or fragment of said ..." might resolve this issue. Claims 28 to 37 are vague and indefinite in so far as they depend from claim 27 for this element.

13.2) Claim 28 is vague and indefinite because SEQ ID NO:31 of the instant application is a nucleotide sequence.

13.3) Claim 37 is vague and indefinite because there is no antecedent basis for "the" "polypeptide encoded by the nucleic acid molecule".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14) Claims 27, 28 and 32 to 36 are rejected under 35 U.S.C. 102(b) as being anticipated by the Buck et al. publication (CELL 65:175-187, 05 Apr. 1991). Claim 27 encompasses an isolated nucleic acid molecule encoding a fragment of a Drosophila Odorant Receptor and that encodes a protein "which causes the firing of an olfactory neuron when stimulated". Because a fragment of a Drosophila Odorant Receptor can consist of as little as a single amino acid, claim 27 encompasses any isolated nucleic acid that encodes a protein which causes the firing of an olfactory neuron when stimulated, including the cDNA clones that were described in Figure 6 on page 180 of the Buck et al. publication long before the making of the instant invention.

With respect to the specific limitations of claim 28, a review of the amino acid sequences presented in Figure 6 of Buck et al. shows that every sequence described therein has at least a conserved Leucine in the extracellular domain, a conserved Proline in the second intracellular domain and a conserved Leucine in the third extracellular domain.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15) Claims 27, 28 and 31 to 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Buck et al. publication cited above. In so far as these claims distinguish over the cDNAs of BUCK et al. in requiring the presence of one or more expression control elements and the production of a protein encoded by the recited nucleic acid, the incorporation of a cDNA of Buck et al. into an expression system for the purpose of producing the protein encoded thereby to facilitate the further characterization of that protein by employing those methods that were very old and well known in the art of molecular biology at the time that the instant invention was made would have been *prima facie* obvious to one of ordinary skill in that art in view of Buck et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JOHN ULM
PRIMARY EXAMINER
GROUP 1800